

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

1. (original) A method of producing a substance or mixture for use in spheroid formation, the method comprising heat treatment of Fetal Calf Serum for a time and at a temperature sufficient to impart spheroid-forming activity to the resultant substance or mixture.
2. (original) A method according to Claim 1, wherein the heat treatment is performed at a temperature between 60°C and 80°C.
3. (previously presented) A method according to Claim 1, wherein the heat treatment is performed at a temperature between 65°C and 75°C.
4. (previously presented) A method according to Claim 1, wherein the heat treatment is performed for between 30 minutes and 12 hours.
5. (previously presented) A method according to Claim 1, wherein the heat treatment is performed at a temperature of 70°C for about five hours.
6. (previously presented) A method according to Claim 1, further comprising the step of storing the resultant substance or mixture in aliquots at about -20°C.

7. (previously presented) A substance or mixture for use in spheroid preparation formed by the method according to Claim 1.

8. (previously presented) A method of spheroid formation comprising contacting in a vessel a cell culture with a substance or mixture formed by the method of Claim 1.

9. (original) A method according to Claim 8, wherein the spheroid-forming substance or mixture is coated on the vessel.

10. (original) A method according to Claim 8, wherein a 5 to 10% solution of the spheroid-forming substance or mixture is added to a medium of the cell culture.

11. (previously presented) A method according to Claim 8, wherein the cell culture comprises more than one cell type, whereby a hetero-spheroid is formed.

12. (currently amended) An elongate spheroid, formed using the substance or mixture of claim 7, comprising a plurality of cells arranged linearly.

13. (original) An elongate spheroid according to Claim 12 which has a length of at least 1cm.

14. (previously presented) An elongate spheroid according to Claim 12, which contains 100,000- 200,000 cells per cm length.

15. (previously presented) An elongate spheroid according to Claim 12, comprising more than one cell type.

16. (previously presented) An elongate hetero-spheroid according to Claim 12, comprising an elongate core of cells of one

type with one or more layers of cells of a different type arranged around said core.

17. (original) An elongate hetero-spheroid comprising MCF7 and breast fibroblast cells.

18. (currently amended) A method of forming an elongate spheroid comprising ~~[[form]]~~ forming a suspension by contacting a cell culture with a spheroid-forming substance or mixture at the required concentration, placing the suspension in a tubular member, incubating the contents of the tubular member, and removing the elongate spheroid.

19. (original) A method according to Claim 18, wherein the required concentration is in the range of 6 to 10 million cells/ml.

20. (previously presented) A method according to Claim 18, wherein the tubular member has an internal diameter of about 1mm.

21. (previously presented) A method according to Claim 18, further comprising the step of stretching the tubular member prior to the incubation.

22. (original) A kit for forming elongate spheroids comprising a spheroid forming substance or mixture and a tubular member.

23. (previously presented) The use of a spheroid-forming substance or mixture formed by the method of Claim 1 in anti-cancer therapy.

24. (original) A polymeric protein comprising a polymer of one or more proteins contained in fetal calf serum, having a molecular weight in excess of 2MDa and having spheroid forming activity.

25. (original) A polymeric protein obtainable by heat treatment of fetal calf serum, whereby said polymeric protein is capable of spheroid forming activity.

26. (previously presented) The use of a polymeric protein according to Claim 24 for the production of spheroids for tissue culture.

27. (previously presented) The use of a polymeric protein according to Claim 24 for the production of spheroids made up of one or more of fibroblasts, smooth muscle cells and bladder cancer cells.

28. (previously presented) The use of a polymeric protein according to Claim 24 for the preparation of skin cells selected from the group comprising keratinocytes and fibroblasts, for use in wound healing and/or skin grafting.

29. (currently amended) A method of elongate spheroid formation, which comprises providing an elongate culture vessel having a generally V-shaped lower cross-section, introducing into said culture vessel a cell culture and a spheroid-forming substance or mixture according to claim 7, incubating the contents of said vessel and removing the elongate spheroid.

30. (original) A method of producing a spheroid making up a grid structure, which comprises providing a corresponding culture vessel defining a grid in which the grid elements are of V-section, and introducing into said culture vessel a cell culture and a spheroid-forming substance or mixture, incubating the contents of said vessel and removing a spheroid of grid-like structure.

31. (previously presented) A method according to Claim 29, wherein said incubation is for a period of 24 to 36 hours.

32. (previously presented) A method according to Claim 29, wherein said V-shaped section defines an inclined angle in the range of from  $20^{\circ}$  to  $120^{\circ}$ .

33. (original) A kit for forming elongate spheroids or a grid-like structure thereof, comprising a culture vessel having an elongate portion with a generally V-shaped lower cross-section, and a spheroid-forming substance or mixture.

34. (previously presented) A method of spheroid formation comprising contacting in a vessel one or more cell cultures with a polymeric protein according to Claim 24.